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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/491,549	01/26/2000	DAVID CHARLES BAULCOMBE		8682

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[REDACTED] EXAMINER

PARAS JR, PETER

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29

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/491,549	BAULCOMBE ET AL.
	Examiner Peter Paras, Jr.	Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE \_\_\_\_ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) Responsive to communication(s) filed on 05 March 2003.
- 2a) This action is **FINAL**.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) Claim(s) 1,5-7,9-15,17,21 and 32-34 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_ is/are allowed.
- 6) Claim(s) 1,5-7,9-15,17,21 and 32-34 is/are rejected.
- 7) Claim(s) \_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_ is: a) approved b) disapproved by the Examiner.  
 If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_ .  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
 \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
 a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |                                                                                               |                                                                             |
|-----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                              | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)          | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ . | 6) <input type="checkbox"/> Other: ____ .                                   |

Applicant's amendment received on 3/5/03 has been entered. Claims 1, 9-12, and 17 have been amended. Claims 8, 16, and 26-29 have been cancelled. Claims 1, 5-7, 9-15, 17, 21, and 32-34 are pending and are under current consideration.

***Priority***

Applicant's arguments regarding the priority claim have been carefully considered. Applicants have argued that the priority claim in the originally filed declaration meets all of the requirements recited in the MPEP. Applicants submit that by specifying the application number, country, day, month and year of its filing (as was done in the original declaration) the requirements to a claim for foreign priority have been met. See the amendment on page 5.

In response, the Examiner asserts that while Applicants have complied with the above stated requirements, the foreign priority claim as recited in the original declaration has been made under an incorrect statute, 37 U.S.C. 119. A claim to foreign priority should be made under 35 U.S.C. 119. For accuracy of the record, a substitute declaration, with a correct claim for foreign priority under 35 U.S.C. 119, should be submitted. See pages 2-3 of the Office action mailed on 8/28/02.

Applicant's amended priority statement, submitted in the amendment received on 3/5/03 has been entered into the specification, immediately following the title of the invention.

***Claim Rejections - 35 USC § 112, 1<sup>st</sup> paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-7, 9-15, 17, 21 and 32-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting silencing of a target gene in a plant, wherein the presence of short RNA molecules (SRMs), which are 21-25 nucleotides in length and share sequence identity with a target gene is correlative with silencing of a target gene, and wherein the silencing of a target gene is also correlative to a phenotype exhibited by said plant, and wherein silencing of a target gene corresponds to the presence of an exogenous nucleic acid molecule, including RNA viruses and transgenes; and a method for isolating SRMs, specific for a target gene, from plants does not reasonably provide enablement for all other methods as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The previous rejection is maintained for the reasons of record advanced on pages 3-12 of the Office action mailed on 8/28/02.

Applicant's arguments filed 3/5/03 have been fully considered but they are not persuasive. Applicants submit that the claims as amended correspond with the subject matter acknowledged as enabled by the Examiner with the exception of two respects. The first being instances where the silencing of a target gene is correlative to a phenotype exhibited by a plant. The second being instances where the target gene is a

transgene or endogenous gene that is the same as a transgene. Applicants argue that these two issues would unduly limit the invention. Applicants further argue that a viral genome may not be considered a transgene, and therefore may not include situations of viral-silencing by a plant. Applicants further argue that although exogenous nucleic acid is one way to initiate silencing it is not an essential feature of the presently claimed invention. See pages 7-8 of the amendment.

In response, the Examiner maintains that the guidance presented by the evidence of record correlates the presence of SRMs with the presence of exogenous nucleic acid molecules. See page 5 of the Office action mailed on 8/28/02. The specification on page 2, lines 16-19 clearly states that the accumulation of 25 nucleotide species of RNA molecules (referred to as SRMs in lines 22-25) required either transgene sense transcription or RNA virus replication. Moreover, the working examples, demonstrating gene silencing, provided by the specification correlate exogenous nucleic acid molecules that are known with the detection of SRMs. See pages 22-27 of the specification. It is clear that transgenes or RNA viruses are exogenous nucleic acid molecules. In the absence of a definition of transgene provided by the specification, the Examiner, in the previous office action, had broadly interpreted the term transgene to encompass all exogenous nucleic acid molecules, including viruses. However, to prevent further confusion, the Examiner has changed enabled scope of the invention to read on exogenous nucleic acid molecules, which would include transgenes and RNA viruses.

With regard to the rejection of claims 1, 5-7, 21 and 32-34, Applicants have argued that it is clear from the claims as originally filed that a degree of homology exists between the SRMs and the target gene in contrast to the Examiner's assertions that the claims should recite that detected SRMs must be specific for the target sequences. However, Applicants submit that the claims as amended now recite a step for determining the degree of sequence identity or similarity between the SRMs and the target gene. See pages 8-9 of the amendment.

In response, the Examiner asserts that although the claims now recite a characterizing step to assess sequence similarity, the claims lack a correlation between any identified SRMs having sequence homology with a target gene and the occurrence of gene silencing. The claims as written merely correlate the presence of SRMs, but not sequence identity of SRMs for a target gene, with the occurrence of gene silencing. See pages 5-6 of the office action mailed on 8/28/02. However, the guidance provided by the instant specification has correlated the presences of SRMs with the presence of exogenous nucleic acid molecules, wherein the exogenous nucleic acid molecule was known having a sequence correlatable to a SRM. For example, Hamilton et al support the Examiner's position relating to exogenous nucleic acid molecules by teaching that exogenous ACO or 35S- $\beta$ -glucuronidase cDNA correlated to gene silencing and the presence of SRMs; the SRMs were correlatable to a known sequence. It does not appear that the specification has provided guidance, which correlates gene silencing and the presence of SRMs with unknown nucleic acid molecules. See pages 6 of the Office action mailed on 8/28/02. It is maintained that evidence of record has not

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correlated the presence of SRMs with silencing of (previously) unknown nucleic acid molecules as a means of identifying silenced genes or the occurrence thereof. Unless a SRM can be correlated to a target gene by sequence there does not appear be any direct connection to silencing such that the skilled artisan would be able to determine if silencing has occurred by the mere presence of SRMs. It is maintained that it would be unpredictable to determine if gene silencing has occurred without sequence correlation between a SRM and a target gene. See pages 6-7 of the Office action mailed on 8/28/02.

Applicants have argued that it is not necessary that the presence of SRMs be correlated to a phenotypic change associated with gene silencing. Applicants submit that gene silencing can be detected without correlation to phenotype. Applicants assert that the detection of SRMs alone is a sufficient indicator of gene silencing.

In response, the Examiner asserts that the guidance provided by the specification correlated the presence of SRMs with introduction of known exogenous nucleic molecules into plants. However, the guidance provided by the evidence of record has not correlated the presence of SRMs with the silencing of any random, unknown gene. If it is not apparent which gene is silenced then how can it be asserted that a gene has been silenced by the presence of SRMs alone, absent phenotypic changes in a plant. Hamilton et al report that two to three weeks after introduction GFP fluorescence was not detectable in a *Nicotiana benthamiana* exhibiting PTGS. See page 7 of the Office action mailed on 8/28/02. In such a case, gene silencing correlated with a phenotypic change. In a situation where a plant does not exhibit a phenotypic

change why would the skilled artisan expect to detect SRMs, which correlate to gene silencing? The evidence of record has not provided any guidance to that end. Furthermore, the specification has contemplated that the gene silencing technology embraced by the instant invention can be used to silence any gene deemed appropriate in order to eliminate or reduce unwanted traits. Such contemplations clearly read on a phenotypic consequence resulting from gene silencing. See pages 10-11 of the specification. It is maintained that in the absence of a phenotypic change the skilled artisan would not understand that a gene is silenced in a plant and would not attempt to detect SRMs. See page 8 of the Office action mailed on 8/28/02.

With regard to the rejection of claims 9-10, Applicants again argue, see above, that a phenotypic change is not required to detect gene silencing.

In response, Examiner maintains that without a phenotypic change as an indication of target gene silencing, it is unpredictable if a target gene has been silenced. See above and as discussed on pages 8-9.

With regard to the rejection of claim 11, Applicants submit that the instant methods are enabled for detection of endogenous as well as exogenous genes. See page 10 of the amendment.

In response, the Examiner asserts that the evidence of record has only provided guidance that correlates detection of SRMs with introduction known exogenous nucleic acid molecules in a plant (see above). The evidence of record has not correlated detection of SRMs, correlatable to gene silencing, in the absence of exogenous nucleic acid molecules in a plant. The state of the art, suggests that PTGS results from the

introduction of exogenous nucleic acid molecules in plants. See pages 9-10 of the Office action mailed on 8/28/02; see Hamilton. The Examiner acknowledges that claim 11 as amended now reads on plants.

Applicants assert that SRMs correspond to gene silencing as related to the rejection of claims 12-15.

The claims as amended read on isolating SRMs from a plant. However, it is unpredictable if SRMs can be isolated from any plant, particularly a plant in which a correlation between gene silencing and phenotypic change is not observed. See above. The Examiner acknowledges that the claims as amended now read on plants.

Applicants have amended claim 17 to now read on plants.

The Examiner acknowledges the amendments to claim 17. The Examiner submits that the aspects of the rejection relating to sequence specificity of SRMs and correlation of gene silencing and SRMs with a phenotypic change in a plant were inadvertently not reiterated under the claim 17 section of the instant rejection. However, in view of the enabled scope of the invention (see above and also in the previous Office action.) and the discussions of the instant Office action and the previous Office action, it is clear that rejections relating to sequence specificity of SRMs and correlation of gene silencing and SRMs with a phenotypic change in a plant apply to claim 17 as well. Any confusion is regrettable.

### **Conclusion**

**No claim is allowed. The claims appear to be free of the prior art but are subject to other rejections.**

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Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at 703-305-4051. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703) 308-4242 and (703) 305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to Dianiece Jacobs whose telephone number is (703) 305-3388.

Peter Paras, Jr.

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**PETER PARAS  
PATENT EXAMINER**

